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BY: Christine Clarke-Robinson DATE: 7/21/00

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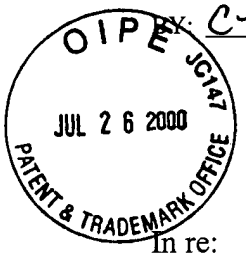

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re:	Patent Application of Douglas E. Kligman, et al.	: Group Art Unit: 1615
Appln. No:	09/131,076	: Examiner: S. Tran
Filed:	August 7, 1998	:
Title:	COMPOSITION AND METHOD OF EFFECTING SUPERFICIAL CHEMICAL SKIN PEELS	: Attorney Docket : No. 10052-1U1

REQUEST FOR RECONSIDERATION

In response to the Office Action dated March 30, 2000 (Paper No. 10), please consider the following remarks. A petition for a one month extension of time and the appropriate fee is enclosed with this request. Accordingly, this Response is timely filed before July 30, 2000.

Claims 1-22 are currently pending in the present patent application.

Presently pending claims 1-7, 11-14 and 20-22 stand rejected by the Examiner, and claims 8-10 are objected to as depending from a rejected base claim. Each of the Examiner's bases for rejection and objection are addressed in detail below.

Invention

The present invention is a method for effecting a superficial chemical skin peel by topically applying a composition comprising a solution of salicylic acid containing at least 15% by weight of salicylic acid in a dermatologically acceptable liquid solvent. The methods of the invention are useful in the treatment of skin disorders which can be treated by exfoliation

(peeling) of the skin's entire surface, such as photodamaged skin, hyperpigmentation, mottled spots, liver spots, age spots, freckles, and/or wrinkled, rough or weathered skin and premalignant neoplasms such as actinic keratoses.

I. Rejection Under § 103(a) over U.S. Patent No. 4,318,907

The Examiner has rejected claims 1-7, 11, 12, 14, 20-22 as being unpatentable over U.S. Patent No. 4,318,907 to Kligman et al. ("Kligman"). Specifically, the Examiner contends that Kligman teaches a composition and procedure for treating acne vulgaris using a composition containing salicylic acid dissolved in aqueous ethanol which, in combination with "routine experimentation" of one of ordinary skill in the art, renders obvious the present invention. Applicants respectfully disagree with the analysis of the Examiner and traverse this objection for the reasons outlined below.

In particular, the Examiner's argument is improper as it fails to meet the requirements of a showing of *prima facie* obviousness, for there is no suggestion or motivation in the art to modify Kligman in the manner the Examiner has proposed. In fact, the opposite is true; a person of ordinary skill in the art would be discouraged from making such modifications as (1) Kligman itself teaches away from the modifications proposed by the Examiner, and (2) even in the absence of such teachings to the contrary, there is no reasonable expectation that such modification of the Kligman disclosure would be successful.

Kligman discloses methods and compositions for the treatment of acne vulgaris that employ a composition containing salicylic acid and benzoyl peroxide dissolved in 75% ethanol and 25% water. (Column 1, lines 5-7). The Kligman composition is intended to be used at home and applied twice daily. (Column 5, line 65). As disclosed in Kligman, the purpose of the disclosed composition is to simultaneously remove the keratinaceous plugs clogging the skin's

follicles, (column 1, lines 29-32), while suppressing the acne bacillus. (Column 2, lines 3-5). Kligman further teaches that the combination of salicylic acid and benzoyl peroxide at disclosed "specified levels" exhibits a therapeutic effect "greater than either agent alone in treating acne." (Column 1, lines 45-51). The "specified level" of salicylic acid taught by Kligman has as its upper limit about 7% by weight of salicylic acid. (Column 2, lines 53-55). Kligman unambiguously states that "the concentration of . . . salicylic acid employed in [the Kligman] invention is important. . . . [Ten percent] salicylic acid with 5% benzoyl peroxide caused excessive redness and peeling . . . and is therefore of little, if any, value in this connection." (emphasis added).

In contrast, the present invention relates to a composition useful for superficial chemical peels that contains at least 15% by weight salicylic acid in a dermatologically acceptable liquid solvent, such as aqueous ethanol. Such composition intentionally provides a superficial chemical peel that removes the epidermis by desquamation of the epithelium, the desired result being the wounding and peeling of the treated skin.

Contrary to the Examiner's assertion, it would not be obvious to a person of ordinary skill in the art to modify Kligman in the manner the Examiner described to arrive at the present invention. To do so would render Kligman unsatisfactory for its intended purpose, namely the non-peeling treatment of acne vulgaris. Furthermore, such modification would be directly contrary to the teachings of Kligman itself. Kligman unambiguously teaches that the concentration of salicylic acid in the composition should not exceed 7% by weight, preferably 5% by weight, because, at higher concentrations, "excessive redness and peeling" result. (Column 2, lines 45-52). In fact, Kligman expressly states that use of salicylic acid in concentrations over 7% by weight is "of little, if any value." (*Id.*).

In contrast, the concentration of salicylic acid in the present invention contains at least 15% by weight of salicylic acid, and in some embodiments, may contain as much as 30% by weight. Such a high concentration, significantly higher than the concentrations of Kligman, would clearly cause redness, irritation and peeling of the skin, the desired result of the claimed invention. Thus, Kligman clearly discourages or "teaches away" from the compositions of the present invention which contain at least 15% by weight of salicylic acid. Accordingly, it would not be obvious for a person of ordinary skill in the art to modify Kligman by routine experimentation and arrive at the present invention.

Even if the Kligman disclosures which "teach away" from the present invention are ignored, which they cannot be, there is no suggestion or motivation to a person of ordinary skill in the art to modify Kligman as proposed by the Examiner, as such modification would make the composition of Kligman highly unsatisfactory for its intended purpose. The disclosure of Kligman requires a concentration of 7% by weight, preferably 5% by weight, of salicylic acid. At this lower level of concentration, the salicylic acid is able to accomplish the intended purpose of the Kligman composition, namely, to promote the expulsion of and prevent the formation of horny masses which clog follicles and to enhance the effects of benzoyl peroxide, also present, without excessive redness and peeling. Modifying Kligman by increasing more than two-fold the salicylic acid concentration to arrive at the at least 15% weight concentration of the present invention would result in a composition causing redness, irritation and wounding of the treated skin, thereby making such composition unsatisfactory for the treatment of acne vulgaris. Kligman, at the time of his prior patent for the treatment of acne vulgaris, simply did not recognize the advantages of the skin peeling composition of the present invention.

Modifications of Kligman by increasing the salicylic acid concentration, therefore, cannot be the basis of an obviousness rejection.

Finally, a person of ordinary skill in the art would have no basis for modifying Kligman as suggested, as there is no reasonable expectation that such modification would be successful. Specifically, if the low salicylic acid concentration required by Kligman were increased to the at least 15% by weight of the present invention, the total amount of salicylic acid would be insoluble in the 25% water/75% ethanol solution of Kligman. Further, as discussed above, a composition containing 15% salicylic acid would not have been thought to be successfully used to treat acne vulgaris because of the undesirable side effects of irritation and wounding of the treated skin.

In addition, there was no reasonable expectation that an increase in the concentration of ethanol in the solution of the Kligman composition would be successful. Ethanol is well known by persons of ordinary skill in the art to be significantly more volatile than water; at the high ethanol concentrations (95% to 100%) required when using at least 15% by weight of salicylic acid, the ethanol will evaporate quickly from the treated skin leaving precipitated salicylic acid crystals. Such almost immediate precipitation would be counter-productive to an acne treatment, as it would sharply limit the amount of time in which the salicylic acid could penetrate into the clogged follicles. Accordingly, there was no reasonable expectation that the modifications to Kligman suggested by the Examiner would be successful.

Thus, the Examiner has failed to make a *prima facie* case of unpatentability under § 103(a) in light of Kligman. Accordingly, reconsideration and withdrawal of the rejection of claims 1-7, 11, 12, 14 and 20-22 is respectfully requested. Further, as claims 8-10 depend, either

directly or indirectly, from the above-listed claims, the withdrawal of the objection to these claims is also requested.

II. Rejection Under § 103(a) over U.S. Patent No. 5,730,991

The Examiner has rejected claims 1-4 and 11-14 as being unpatentable over U.S. Patent No. 5,730,991 to Rapaport ("Rapaport"), which the Examiner contends discloses a skin peel for topical application comprising salicylic acid in acetone. Specifically, the Examiner contends that it would have been obvious for one of ordinary skill in the art to modify the amount of salicylic acid disclosed in Rapaport to arrive at the present invention. Applicants respectfully disagree with the Examiner, and traverse this rejection for reasons outlined below.

Rapaport teaches methods and compositions for use in an at-home skin peel comprising a first degreasing step, and a second peeling or exfoliating step that requires topical application of a solution containing low concentrations of a peeling/exfoliating agent such as salicylic acid. As disclosed, this peeling/exfoliating agent may be salicylic acid in concentrations of 0.1% to 5% by weight, it may be acetone in concentrations of 0.1% to 10% by weight, or both. The presence of acetone in the composition of Rapaport is required, as it is alleged to be a penetration enhancer that increases the effects of the other selected peeling/exfoliating agent(s), also present in low concentration(s). Rapaport notes that low concentrations of acetone are required because application of higher concentrations of acetone result in blistering and irritation of the skin. (Column 1, line 44). Avoidance of high concentrations of acetone is required by Rapaport, as the disclosed composition itself is advantageous precisely because it is not "irritating or wounding [to] the skin." (Column 8, lines 38-40).

In contrast, the methods of the presently claimed invention comprise at least 15% by weight of salicylic acid in a dermatologically acceptable liquid solvent. Low concentrations of salicylic acid, such as those discussed in Rapaport, are not significantly efficacious for the application of the claimed invention. Further, concentrations of liquid solvent which are lower than the concentration necessary to solubilze the at least 15% by weight of salicylic acid, such as the 0.1% to 10.0% acetone by weight acetone recited by Rapaport, are also unacceptable for use in the present invention.

There is no motivation or suggestion in the art that would cause a person of ordinary skill in the art to undertake the modification of Rapaport as proposed by the Examiner to arrive at the claimed invention. Rapaport teaches uses of low concentrations of acetone and salicylic acid for use in skin peels. Such low concentrations, Rapaport teaches, are necessary in order to accomplish the end result of a low strength chemical peel for take home use, which can be applied more than once daily and which results in no wounding or perceptible irritation of the skin. Modification of Rapaport to contain the at least 15% salicylic acid concentration of the present invention would be contrary to the teachings of Rapport, as the resulting composition would wound and irritate the skin. Further, the at least 15% salicylic acid of the present invention is not completely soluble in the low acetone concentrations disclosed by Rapaport. One would have to further modify Rapport by increasing the concentration of acetone to arrive at the present invention. The resulting composition would again cause irritation and inflammation of the treated skin. This is again contrary to the teachings of Rapaport and would render it unsatisfactory for its intended use, namely, at home skin peels which cause no perceptible irritation or wounding of the skin.

It is respectfully submitted that the Examiner has failed to present a *prima facie* case of obviousness in light of the disclosure of Rapaport. Accordingly, reconsideration and withdrawal of the rejection of claims 1-4 and 11-14 is respectfully requested. Further, as claims 8-10 depend, either directly or indirectly, from the above-listed claims, the withdrawal of the objection to these claims is also requested.

CONCLUSION

In light of the forgoing remarks, reconsideration and withdrawal of the Examiner's rejections and objections are respectfully requested, and allowance of said claims is earnestly solicited.

Respectfully submitted,

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24 July 2000
(Date)

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